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*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*

(54) Title: MODIFIED NUCLEOTIDES FOR POLYNUCLEOTIDE SEQUENCING

(57) Abstract: The invention provides modified nucleotide or nucleoside molecule comprising a purine or pyrimidine base and a ribose or deoxyribose sugar moiety having a removable 3'-OH blocking group covalently attached thereto, such that the 3' carbon atom has attached a group of the structure -O-Z wherein Z is any of -C(R')<sub>2</sub>-O-R", -C(R')<sub>2</sub>-N(R'')<sub>2</sub>, -C(R')<sub>2</sub>-N(H)R", -C(R')<sub>2</sub>-S-R" and -C(R')<sub>2</sub>-F, wherein each R" is or is part of a removable protecting group; each R' is independently a hydrogen atom, an alkyl, substituted alkyl, arylalkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclic, acyl, cyano, alkoxy, aryloxy, heteroaryloxy or amido group, or a detectable label attached through a linking group; or (R')<sub>2</sub> represents an alkylidene group of formula =C(R''')<sub>2</sub> wherein each R''' may be the same or different and is selected from the group comprising hydrogen and halogen atoms and alkyl groups; and wherein said molecule may be reacted to yield an intermediate in which each R" is exchanged for H or, where Z is -C(R')<sub>2</sub>-F, the F is exchanged for OH, SH or NH<sub>2</sub>, preferably OH, which intermediate dissociates under aqueous conditions to afford a molecule with a free 3'OH; with the proviso that where Z is -C(R')<sub>2</sub>-S-R", both R' groups are not H.



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# INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C07H19/06 C07H19/10 C07H19/16 C07H19/20 C07H21/00  
C12Q1/68 G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C07H C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/29003 A (UNIV COLUMBIA) 11 April 2002 (2002-04-11) the whole document	1,6-11, 29-50
X	US 6 255 475 B1 (KWIATKOWSKI MAREK) 3 July 2001 (2001-07-03) figure 4 examples claims the whole document	1,2, 8-10,29
X	J. BRUNCKOVA ET AL.: "Intramolecular hydrogen atom abstraction in carbohydrates and nucleosides" TETRAHEDRON LETTERS, vol. 35, 1994, pages 6619-6622, XP002270558 compound 10a-c	1,2
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/03686

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	S. NISHINO ET AL.: "Efficient deanilidation of phosphoranilidates by the use of nitrites and acetic anhydride" HETEROATOM CHEMISTRY, vol. 2, 1991, pages 187-196, XP008027710 scheme 2	1,2
X	----- M. KRECEROVA ET AL.: "Synthesis of 5'-O-phosphonomethyl derivatives of pyrimidine 2'-deoxynucleosides" COLL. CZECH. CHEM. COMMUN., vol. 55, 1990, pages 2521-2536, XP002270559 the whole document	1,5
X	----- P.J.L.M. QUAEDFLIEG ET AL.: "An alternative approach towards the synthesis of (3'-5') methylene acetal linked dinucleosides" TETRAHEDRON LETTERS, vol. 33, 1992, pages 3081-3084, XP002270560 the whole document	1,5
X	----- J.-I. YAMASHITA ET AL.: "Studies on antitumor reagents. VII. Antitumor activities of O-alkoxyalkyl derivatives of 2'-deoxy-5-trifluoromethyluridine" CHEM. PHARM. BULL., vol. 35, 1987, pages 2373-2381, XP002270561 tables	1,2,5
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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 03/03686

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>US 2003/104437 A1 (BALASUBRAMANIAN SHANKAR ET AL) 5 June 2003 (2003-06-05)</p> <p>the whole document -----</p>	<p>1,2, 5-11, 29-50</p>

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/03686

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-2, 5-11, 29-50 ( all in part )

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-2, 5-11, 29-50 (all in part)

A modified nucleotide or nucleoside molecule as claimed in claim 1 where Z is  $-C(R')_2-O-R''$  with  $R'$  and  $R''$  as defined in claim 1, and methods and kits pertaining thereto.

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2. claims: 1-2 (in part), 3-4 (in full), 5-11 (in part), 29-50 (in part)

A modified nucleotide or nucleoside molecule as claimed in claim 1 where Z is  $-C(R')_2-N-(R'')_2$ , or  $-C(R')_2-N(H)R''$ , or  $-C(R')_2-N_3$  with  $R'$  and  $R''$  as defined in claim 1, and methods and kits pertaining thereto.

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3. claims: 1-2, 5-11, 29-50 (all in part)

A modified nucleotide or nucleoside molecule as claimed in claim 1 where Z is  $-C(R')_2-S-R''$  with  $R'$  and  $R''$  as defined in claim 1, and methods and kits pertaining thereto.

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4. claims: 1-2, 5-11, 29-50 (all in part)

A modified nucleotide or nucleoside molecule as claimed in claim 1 where Z is  $-C(R')_2-F$  with  $R'$  as defined in claim 1, and methods and kits pertaining thereto.

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5. claims: 12-15 (in full), 29-50 (in part)

A nucleoside, nucleotide or polynucleotide molecule as claimed in claim 12, and methods and kits pertaining thereto.

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6. claims: 16-28 (in full)

A method of converting as claimed in claim 16 and the molecule of claim 20.

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International Application No

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International Application No  
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